University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-32 Sleep Disorder Agents

Effective Date: 6/26/24

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plan and may not be covered by all UM Health Plan plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact UM Health Plan Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Health Plan covers sleep disorder medications including Sunosi (solriamfetol), Lumryz (sodium oxybate), Wakix pitolisant), and Xywav (oxybate Salts) when prior authorization criteria are met. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of adverse effects, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General considerations for use

A. Appropriate medication use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designate signs, symptoms, and test Results to support specific diagnosis.

2. Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved use: Compendium support (UpToDate® Lexidrug™) for use of a drug for a non-FDA approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

II. Obstructive Sleep Apnea [must meet all listed below]:

A. Age: at least 18 years.

B. Diagnosis and severity.

1. Etiology: obstructive apneas, hypopneas, or respiratory efforts-related arousals.

2. Symptoms: witnessed apnea; snoring; gasping/choking; excessive sleepiness not explained by other factors; non-refreshing sleep; sleep fragmentation; insomnia; morning headache(s); decreased concentration; memory loss; decreased libido; irritability.

C. Polysomnography confirmation [must meet both listed below]:

1. In conjunction with appropriate Positive Airway Pressure titration.

2. Apnea Hypopnea Index value [must meet one listed below]:

a. With symptoms: At least five per hour in conjunction with symptoms of daytime sleepiness, loud snoring, witnessed apneas, or awakening due to gasping/choking.

b. No symptoms: At least fifteen per hour without symptoms.

D. Other therapies: Trials of each pertinent category listed below are required unless contraindicated. Trials must result in an inadequate response after four months of consistent use or a severe adverse reaction.

1. Central nervous system stimulants [must meet both listed below]:

a. Modafinil: 100 to 200 mg per day (quantity limit of one per day).

b. Armodafinil: 150 to 250 mg per day (quantity limit of one per day).

2. OSA with allergic rhinitis [must meet one listed below]:

a. Nasal steroids.

3. Continuous Positive Airway Pressure [must meet both listed below]:

a. Maximized therapy: used for over four hours per night for over 70 percent of the nights.

b. Rule out CPA issues: mask fit, humidity, ramp, repair, need for alternative Positive Airway Pressure (PAP) modality, pressure leaks, or inadequate pressure.

E. Dosage regimen.

1. Sunosi oral (solriamfetol): 37.5mg per day (half 75mg tab); then, based on response and tolerability, may double the dose at least three-day intervals to a maximum dose of 150mg per day.

F. Approval.

1. Initial: six months.

2. Re-approval:

    a. Continue to meet the criteria for obstructive sleep apnea.

    b. Duration: six months to one year.

III. Narcolepsy with or without cataplexy [must meet all listed below]:

A. Age: 7 to 64 years.

B. Prescriber: neurologist, psychiatrist, or sleep medicine specialist.

C. Narcolepsy type 1: narcolepsy with cataplexy [must meet all listed below]:

1. Diagnosis and severity [must meet both listed below]:

    a. Presence of excessive daytime sleepiness for more than three months.

    b. Cataplexy: loss of muscle tone in full consciousness triggered by emotions.

2. Multiple Sleep Latency Tests confirmation [must meet both listed below]:

    a. Sleep latency: less than eight minutes.

    b. Sleep-onset REM periods: demonstrated in at least two naps after at least six hours of sleep the night before.

D. Narcolepsy type 2 narcolepsy without catalepsy [must meet all listed below]:

1. Diagnosis and severity [must meet all listed below]:

    a. Presence of excessive daytime sleepiness for more than three months.

    b. Variable clinical course with improvement or even disappearance of the symptoms, the development of cataplexy, or a change to idiopathic hypersomnia:

2. Multiple Sleep Latency Tests confirmation [must meet all listed below]:

    a. Sleep latency: less than eight minutes.

    b. Sleep-onset REM periods: demonstrated in at least two naps after at least six hours of sleep the night before.

E. Sunosi other therapies: Trials of each agent listed below are required unless all are contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

1. Modafinil: 100 to 200 mg per day (quantity limit of one per day).

2. Armodafinil: 150 to 250 mg per day (quantity limit of one per day).

3. Methylphenidate or amphetamine analogue.

F. Lumryz, Wakix, and Xywav other therapies: Trials of each agent listed below are required unless all are contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

1. Modafinil: 100 to 200mg per day (quantity limit of one per day).

2. Armodafinil: 150 to 250mg per day (quantity limit of one per day).

3. Methylphenidate or amphetamine analogue.

4. Sunosi.

G. Dosage regimen.

1. Lumryz (sodium oxybate extended release): 4.5 g as a single dose at bedtime. May increase nightly dose by 1.5 g at weekly intervals based on efficacy and tolerability; recommended dosage range: 6 to 9 grams once daily at night. Maximum dose: 9 grams per night.

2. Sunosi (solriamfetol): 75 mg per day, then based on response and tolerability, may double the dose at least three-day intervals to a maximum dose of 150 mg per day.

3. Wakix (Pitolisant): 8.9 mg once daily for 1 week, then increase to 17.8 mg once daily for 1 week; may further increase dose based on response and tolerability during week 3 to a maximum dose of 35.6 mg once daily.

4. Xywav (oxybate salts):

a. Adults: 2.25 g at bedtime after the patient is in bed, and 2.25 g taken 2.5 to 4 hours later (4.5 g/night). May increase nightly dose by 1.5 g (0.75 g at bedtime and 0.75 g 2.5 to 4 hours later) at weekly intervals based on efficacy and tolerability; usual effective dosage range: 6 to 9 grams per night. Maximum dose: 9 grams per night.

b. Pediatrics:

Patient Weight	Initial Dosage		Maximum Recommended Dosage	
	Take at Bedtime	Take 2.5 – 4 Hours Later	Take at Bedtime	Take 2.5 – 4 Hours Later
20 kg to <30 kg	≤ 1 gram	≤ 1 gram	3 grams	3 grams
30 kg to <45 kg	≤ 1.5 gram	≤ 1.5 gram	3.75 grams	3.75 grams
≥45 kg	≤ 2.25 grams	≤ 2.25 grams	4.5 grams	4.5 grams

H. Approval.

1. Initial: six months.

2. Re-approval:

a. Continue to meet the criteria for Narcolepsy.

b. Duration: six months to one year.

IV. Idiopathic Hypersomnia

A. Age: at least 18 years

B. Prescriber: neurologist, psychiatrist, or sleep medicine specialist.

C. Idiopathic Hypersomnia [must meet all listed below]:

1. Diagnosis and severity [must meet both listed below]:

a. Daily periods of irrepressible need to sleep

b. Absense of cataplexy.

c. No evidence of insufficient sleep

d. Confirmatory testing [must meet one listed below]:

i. Polysomnogrphy total sleep time at least 660 minutes

ii. Mean sleep latency less than 8 minutes on multiple sleep latency test.

D. Other therapies: Trials of each agent listed below are required unless all are contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

1. Modafinil: 100 to 200mg per day (quantity limit of one per day).

2. Clarithromycin.

3. Methylphenidate.

E. Dosage regimen: Xywav:

1. Once nightly dosing: Initiate at 3 g or less per night orally, as one dose. Titrate to effect in increments of up to 1.5 g per night per week, up to 6 g total nightly dose.

2. Twice nightly dosing: Initiate at 4.5 g or less per night, divided into two doses. Titrate to effect in increments of up to 1.5 g per night per week, up to 9 g total nightly dose.

F. Approval

1. Initial: six months.

2. Re-approval: one year.

V. Exclusions:

A. Hypersomnia is better explained by other factors (see Appendix I).

1. Other sleep disorders: insufficient sleep syndrome, poor sleep hygiene.

2. Other general disorders/conditions: neurological disorder, mental disorder, thyroid disorder, genetic disorder, inflammatory conditions.

3. Substance: sedating medication use or substance use disorder.

B. Excluded Drugs: Xyrem (sodium oxybate).

1. Trials of all preferred formulary agents are required unless contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

    a. Formulary medications include CNS stimulants (e.g., methylphenidate), modafinil, armodafinil, Sunosi (solriamfetol), Lumryz (sodium oxybate), Xywav (oxybate salts), and Wakix (pitolisant).

C. Inappropriate medication use.

1. Food and Drug Administration (FDA) approval status [must meet one listed below]:

    a. Non-FDA approved: product, indication, and/or dosage regimen without compendium support

2. Place in therapy: sequence of therapy not supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

4.0 Coding:

None.

5.0 References, Citations & Resources:

1. Narcolepsy: Clinical approach to etiology, diagnosis & treatment. Reviews in Neurological Disease 2011;8 (3-4) ;e97-e106.
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3. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Sunosi, Xyrem accessed May 2021.
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5. Central Disorders of hypersomnolence: Focus on the narcolepsies and idiopathic hypersomnia.
6. Screening for Obstructive Sleep Apnea in Adults: An Evidence Review for the U.S. Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017 Jan.
7. Clinical Guidelines for evaluating, managing, and long-term care of obstructive sleep apnea in adults.
8. Journal of Clinical Sleep Medicine 2008;5(3):263-276.
9. Medical therapy for obstructive sleep apnea: A review by the medical therapy for obstructive sleep apnea task force of the standard of practice committee of the American Academy of Sleep Medicine. SLEEP 2006;29(8):1036-1044.
10. Narcolepsy and other central hypersomnias. Continuum 2017;23(4):989-1004.
11. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. J Clin Sleep Med 2021; 17:1895.
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13. European guideline and expert statements on the management of narcolepsy in adults and children. Eur J Neurol 2021; 28:2815
14. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Lumryz, Wakix, Xywav accessed November 2023.
15. UpToDate: Idiopathic hypersomnia [Internet] Accessed November 2023. Available from: http://www.uptodate.com/contents/.
16. Maski K. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. Jornal of Sleep Medicine. September 1, 2021. Accessed November 8, 2023. https://jcsm.aasm.org/doi/10.5664/jcsm.9328.

17. Xywav [package insert]. Palo Alto, CA: Jass Pharmaceuticals, Inc. https://pp.jazzpharma.com/pi/xywav.en.USPI.pdf. Published 4/2023. Accessed 11/2023.

6.0 Appendices:

See pages 8 - 9.

7.0 Revision History:

Original Effective Date: 07/21/2004

Next Review Date: 07/01/2025

Revision Date	Reason for Revision
8/19	Moved to new format; moved dosing, filled in missing criteria under MSLT, replaced abbreviations, clarified dosing
1/20	Off cycle review, changed title; deleted Provigil, Nuvigil from authorization and now are other therapies; added Sunosi and Xyrem; added age and prescriber to narcolepsy criteria.
11/20	Off cycle review, excluded Xyrem, Xywav, added inappropriate medication use under exclusions, approved by P&T Committee 12/9/20
5/21	Annual review clarified criteria instructions and sleep-onset REM periods; eliminated or replaced abbreviations
4/22	Annual review for May workgroup and the June P and T committee; corrected numbering added compendium to appropriate use
4/23	Annual review; added references, clarified inappropriate use
11/23	Off cycle review: addition of Lumryz, Wakix, Xywav for narcolepsy, idiopathic hypersomnia treatment with Lumryz, other therapies language update
4/24	Annual review: removed Monitoring and Patient Safety Table

Appendix I: Differential Diagnosis of Excessive Daytime Sleepiness

Insufficient Sleep	
Sleep deprivation	
Environmental intrusions	
Sleep Disorders	
Obstructive sleep apnea (OSA)	
Central sleep apnea	
Sleep related hypoventilation of hypoxemia	
Central disorders of hyper somnolence:	• Narcolepsy (1 or 2). • Kleine-Levine syndrome. • Idiopathic hypersomnia
Circadian rhythm sleep-wake disorders	• Delayed sleep phase disorder. • Advance sleep phase disorder. • Jet lag, • Shift work
Restless legs syndrome	
Other Neurological Disorders	
Neurodegenerative disease	• Parkinson's disease • Dementia with Lewy bodies • Alzheimer's disease • Multiple system atrophy
Myotonic dystrophy	
Multiple Sclerosis (MS)	
Amyotrophic Lateral Sclerosis	
Structural lesions affecting thalamus, hypothalamus or brainstem	
Traumatic Brain injury	
Encephalitis lethargica	
Cerebral trypanosomiasis	
Medical & Genetic Disorders	
Hypothyroidism	
Obesity	
End-stage renal disease	
Adrenal insufficiency	
Hepatic encephalopathy	
Niemann-Pick Type C	
Prader-Willi syndrome	
Psychiatric Disorders	
Depression	
Anxiety	
Substance abuse: alcohol, narcotics. Rx opioids. stimulant withdrawal	
Psychogenic sleepiness	
Medications	
Benzodiazepines, non-benzodiazepine sedatives, antipsychotics, opioid analgesics, beta blockers (lipophilic), barbiturates, antihistamines, anticonvulsants, sedative antidepressants, muscle relaxers	

Appendix II: Definitions

Term	Definition
Apnea	Cessation of airflow for at least 10 seconds[8,275]
Hypopnea	Reduction in airflow by at least 30% for at least 10 seconds with decrease in oxygen saturation
Apnea-hypopnea index (AHI)[*]	Number of apnea and hypopnea events per hour of sleep
Obstructive sleep apnea (OSA)	
Mild[8,73]	AHI ≥5 to <15
Moderate[8,73]	AHI ≥15 to <30
Severe[8,73]	AHI ≥30
Obstructive sleep apnea syndrome	AHI ≥5 with evidence of daytime sleepiness[3,8,276]

* The respiratory disturbance index (RDI) is a similar measure to AHI, but it also includes the number of respiratory effort–related arousals per hour of sleep (in addition to apnea and hypopnea events).

Abbreviations: AHI=apnea-hypopnea index; OSA=obstructive sleep apnea; RDI=respiratory disturbance index.